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ABSTRACT

This paper summarizes the major advances achieved by research in the fields of infectious diseases and immunizations during the 1970s, and delineates directions for future research in these fields. (Author/MP)

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MATRIX NO. 15

INFECTIOUS DISEASES AND IMMUNIZATIONS

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INFECTIOUS DISEASES AND IMMUNIZATIONS

Major advances were made through research during the 1970s in the fields of infectious diseases and immunizations. Many of these advances already have been transferred to clinical medicine and now are being used for the diagnosis, treatment or prevention of these diseases. Several fatal diseases have been almost completely eliminated, and new treatments are available for other diseases which will benefit millions of children in the future. The use of new immunizations brings hope for the prevention of certain diseases, which, until recently, were without treatment and in some cases were without known cause.

Research in the 1980s offers even greater opportunities for the identification of the causes of the diseases of unknown etiology as well as improved methods for treatment and prevention of recognized infectious diseases. It is fortunate in the case of infectious diseases that many of the causative agents now can be identified and the infections controlled. Others, however, still have eluded detection and further research is required before appropriate health measures can be instituted. Significant opportunities should become available for the prevention and treatment of many diseases of national and international importance. Active basic and clinical research, combined with implementation through clinical medicine and public health procedures, should provide important new advances in the 1980s.

Some of the important advances that were made in the 1970s are listed in Table I. The discovery of methods for detecting and diagnosing hepatitis A and B already have had tremendous beneficial impact on medical care. By testing all units of blood collected at blood banks, it now is possible to exclude hepatitis B containing blood, and thus prevent serum hepatitis that would have been associated with use of this blood in transfusions. These methods already have been adopted as routine procedures utilized in blood banking throughout the United States, and there has been a significant reduction in serum hepatitis. In addition, the availability of tests for detection of hepatitis B permitted the recognition of the problem of exposure of newborns of mothers who were infected with hepatitis B. It now is possible to identify these infected women and to administer hyperimmune gamma globulin to their newborn children. This gamma globulin protects most of the newborns from acquiring hepatitis B infection.

Subacute sclerosing panencephalitis (SSPE), a fatal brain disease of children, was found to be associated with measles virus infection. In most cases the child has had a usual case of measles at a young age and appears perfectly normal for 5 to 10 years. Then, without warning, the child begins to show mental deterioration, inability to walk properly, convulsions, and finally coma and death. Once the symptoms of the brain involvement begin to appear, the average child lives only 1 to 1½ years. This severe brain disease is caused by the measles virus that is harbored in the brain of the child after the acute attack without any apparent effects until a much later date. There is no effective treatment for this tragic illness. Fortunately, however, following the very extensive measles immunization programs in the United States during the 1970s, there was a simultaneous reduction, and now almost complete elimination, of SSPE. It is indeed fortunate that the vaccine strains of measles virus not

TABLE I

Advances In The 1970s

Infectious Diseases

1. Diagnostic methods were developed for hepatitis A and B. Hyperimmune gamma globulin was used to protect exposed newborns from hepatitis B.
2. Subacute sclerosing panencephalitis, a fatal brain infection associated with measles virus infection, was eliminated almost completely.
3. Improved new antibiotics met the challenge of resistant bacteria and special needs.
4. Rotaviruses were found to be major causes of diarrhea of infants and children, and the Norwalk group of viruses was demonstrated to be responsible for a portion of epidemic, nonbacterial gastroenteritis of school age children and adults.
5. Chlamydial infections were shown to cause pneumonia in infants as well as urithritis and pelvic infections in older children and adults.
6. Epstein-Barr virus, the cause of infectious mononucleosis, also was shown to be associated with Burkitt's lymphoma, a childhood malignancy, and nasopharyngeal carcinoma in adults.
7. Legionnaire's disease was shown to be caused by *Legionella* organisms and antibiotics were used for treatment.

Immunizations

1. Smallpox was eradicated throughout the world.
2. Rubella (German measles) immunization was highly successful – no major epidemics since 1964.
3. Measles immunization was effective; only *mini* outbreaks occurred among nonimmunized groups.
4. Polio mass immunization was continued. Only very rare cases of the paralytic disease occurred.
5. Meningococcal vaccines were developed for Groups A and C meningococci.
6. Use of mumps vaccine resulted in a marked decline in this disease.
7. Pneumococcal vaccine was produced for certain high risk groups including children with sickle cell anemia and splenectomized individuals.
8. A new, highly potent, diploid rabies vaccine was developed.

TABLE II

Research Prospects For The 1980s

Infectious Diseases

1. Identification of the cause and possible prevention of Reye's syndrome and Kawasaki disease.
2. Antiviral chemotherapy expanded for herpes infections, hepatitis, shingles, and other severe viral illnesses.
3. Hepatitis B routine testing of certain groups of pregnant women and use of immune globulin for their children.
4. Better understanding of Group B streptococcal disease of the newborn – frequency, treatment, prevention.
5. New antibiotics for special needs including resistant strains of bacteria, Pseudomonas infections in cystic fibrosis, fungal infections.
6. Development of rapid viral diagnostic methods to allow advantage to be taken of new antiviral drugs.
7. Increased understanding of toxoplasmosis and cytomegaloviruses as causes of disease in newborns and children.
8. Better understanding of slow virus diseases and methods for prevention.
9. Prevention of herpes virus infections in the newborn and recurrent herpes in adults.
10. Better control of otitis media based on investigations in experimental animals and children.
11. Further information on Haemophilus influenzae type b meningitis and possible development of a vaccine.
12. Rapid tests for sepsis (bacterial infection in the blood).
13. Improved quality of serological tests for viral antibodies.
14. Prevention of the toxic shock syndrome in older girls and women.
15. Identification of Non A-Non B hepatitis viruses that now cause the majority of posttransfusion hepatitis.

Immunizations

1. Better influenza type A and B vaccines.
2. Meningococcal Group B vaccine.
3. Respiratory syncytial virus vaccine for infants to prevent severe respiratory illness.
4. Enteric viral vaccines to prevent rotaviruses for diarrhea in infants and children.
5. Varicella-zoster (chickenpox) vaccine for high risk groups such as children with malignancies, and possibly for general use.
6. Cytomegalovirus vaccine for immunosuppressed individuals and possibly for general use.
7. Hepatitis vaccines for hepatitis A, B, and Non A, Non B.
8. Vaccine for gonorrhea.
9. Possible immunization against malaria.
10. Improved vaccine for pertussis (whooping cough).
11. Heat stable vaccines for polio and measles.

only prevent measles but also this fatal brain infection caused by measles. Countries where measles immunization is not used continue to report cases of SSPE as in the past.

A number of new antibiotics were introduced in the 1970s. Among the most important were new cephalosporins and aminoglycosides. These new antibiotics met the need for special treatments in patients who did not respond to conventional antibiotics. They were particularly important in life-threatening diseases, such as certain forms of bacterial endocarditis, pneumonia, abdominal infections, bone and joint infections, and neonatal meningitis. With the emergence of resistance of some bacteria to penicillin and other antibiotics, new forms of antibiotics became available in the 1970s to combat these problems. Through the combined efforts of biochemists and microbiologists new *tailor-made* antibiotics were developed and then evaluated by clinical research investigators to determine their usefulness in the treatment of these difficult cases. A *combination* antibiotic, trimethoprim and sulfamethoxazole, also was released which is particularly useful for urinary tract infections, ear infections, and pneumocystis carinii pneumonia that occurs in children who are immunosuppressed by cancer chemotherapy. These research efforts have resulted in a series of new and modified antibiotics to meet the needs of the 1970s and early '80s.

Diarrhea in infants and young children has been recognized as an extremely frequent and sometimes very severe cause of illness. While a small proportion of these cases is caused by bacteria, many have had no known cause. During the 1970s, however, researchers showed that rotaviruses were a major cause of nonbacterial diarrhea in infants and children. Furthermore, the Norwalk group of viruses was shown to cause many of the epidemics of gastroenteritis in school-age children and adults. Recognition of these viruses permitted the development of diagnostic tests to establish the specific causes of the diarrhea in epidemics and in hospitalized children. It is hoped that vaccines will be available for the prevention of some of these illnesses in the near future.

Chlamydial infections have been known to cause conjunctivitis in newborns and adults. It was not until the 1970s that extensive research on Chlamydia using new culture techniques demonstrated that certain serotypes of these organisms cause not only inclusion conjunctivitis but also pneumonia in infants. Apparently the infection is acquired from the mother at the time of birth; fortunately it is limited and responds to proper treatment. In older children and adults, Chlamydia has been shown to be sexually transmitted and to cause urithritis and salpingitis (pelvic infections). Further studies of various antibiotics and other approaches are needed to develop optimal methods for prevention and treatment of these diseases.

Epstein-Barr virus (EBV) has been recognized as the cause of infectious mononucleosis. An association between this virus and the childhood malignancy, Burkitt's lymphoma, and rarely other lymphomas, as well as nasal pharyngeal carcinoma in adults, was demonstrated during the 1970s. Thus, EBV virus is not only the cause of infectious mononucleosis but is also related to at least two types of malignancies.

Legionnaire's disease, an acute pneumonia, which can occur in children but is more frequent in older adults, was shown to be caused by *Legionella* organisms. It was

found that there are at least six related species of this microorganism and in some outbreaks a flu-like illness occurs without pneumonia. The organism also was detected in pools of warm water including cooling towers for air conditioning equipment. Diagnostic tests are available now and antibiotics can be used for treatment.

These advances in the 1970s have shown the importance of basic laboratory research, clinical research, and the transfer of information so acquired to clinical medicine for the treatment and prevention of important infectious diseases in children and young adults.

Great strides were made through immunization in the 1970s. Complete eradication of smallpox throughout the world was a particularly important achievement. For centuries, smallpox had been a dreaded human disease that caused death and left deep scars on the survivors. Epidemics had swept throughout the world at various intervals since earliest times killing many thousands of persons. With the availability of efficient vaccines for smallpox and careful public health measures to vaccinate contact individuals, it was possible to report the total eradication of this disease in the 1970s. Although surveillance must be maintained for many years to come, children no longer have to be immunized for smallpox since the disease has disappeared.

Another remarkable advance in the 1970s was the development of a highly successful rubella immunization program in the United States. It should be remembered that the virus of rubella was first cultured in the early 1960s and that the vaccines were developed in the late 1960s. By intensive use of these vaccines in children and susceptible young adults, it has been possible to reduce the frequency of rubella to very low levels. Thus the epidemics of rubella, which previously occurred every 4 to 10 years, have been stopped. Only minor outbreaks occur among nonimmunized individuals, chiefly young adults. Following the 1964 epidemic of rubella in this country there were more than 20,000 damaged children born with congenital rubella. In recent years there have been less than 50 cases per year. This figure can be reduced even further by greater emphasis on vaccination of susceptible young adults as well as immunization of all children at 12 to 15 months of age. It can be expected that with the continued intensive use of rubella vaccines the severe defects associated with congenital rubella in children born to women who had rubella during pregnancy no longer will be a problem in this country.

Measles immunization was also very effective during the 1970s. This once *common* childhood illness, which is sometimes associated with severe encephalitis and other damage, is now an infrequent infection. Only mini outbreaks occur among nonimmunized groups in this country. It is the goal of the vaccine program to eliminate measles in the United States early in the 1980s.

Polio mass immunization was continued during the 1970s as an extension of programs started in the 1950s and 1960s. Today there are fewer than 10 cases of poliomyelitis each year in the United States. It can be expected that with continued intensive immunization of susceptible individuals this disease will be extremely rare.

The beneficial results in the United States in the control of rubella, measles and polio are not enjoyed by peoples in many other parts of the world. In fact, in most

parts of the world measles, rubella and polio vaccines are not used routinely and the diseases continue to flourish.

Meningococcal vaccines were developed for Groups A and C. These vaccines already have been shown to be of value in epidemics in various parts of the world. Intensive work is continuing on vaccines for Group B, the type which is more common in the United States. A and C vaccines, however, are available and can be used should these forms of this disease occur in this country.

The new mumps vaccine often has been combined with measles and rubella immunization providing *triple* protection for children. The results for the mumps vaccine have been impressive and have reduced significantly the frequency of mumps and mumps-associated illness in the general population.

A pneumococcal vaccine against the 14 most prevalent or invasive types of this bacteria was successfully prepared and released. This is of particular value for children over 2 years of age who have sickle cell anemia, nephrotic syndrome or have been splenectomized, since these patients are at particular risk for infections with pneumococci. The vaccine also is being used for prevention of pneumococcal ear infections in infants and to prevent pneumonia in young adults.

A new human diploid rabies vaccine was developed in the 1970s and was recently released for use. This vaccine is more potent and effective than previous vaccines. Only five injections are needed following an exposure to a rabid animal.

It is fortunate that the vaccines of the 1970s have provided methods for the prevention of major illnesses of children and adults. By continuing to use these vaccines it should be possible to reduce or eliminate these important diseases.

Prospects

With continued intensive research activities aimed at elucidating the basic mechanisms of many poorly understood infections, the prospect in the 1980s is extremely good for the control, prevention and/or elimination of certain infectious diseases.

For Reye's syndrome, it will be important to identify the co-factors involved in this disease. Reye's syndrome usually follows chickenpox or influenza and may result in severe liver damage and brain involvement which can be fatal to the child. Most children with Reye's syndrome are between 4 months and 17 years of age with a mean of 8 years. Overall, approximately one-third of the affected children with this disease die. Very little is known about the reason why certain children experience this severe illness, although it is clear that there is a high concentration of these cases in areas around the Great Lakes, particularly in the states of Ohio and Michigan. One study indicates that aspirin may increase the risk of getting this disease. Intense epidemiological, laboratory and clinical studies will be necessary to identify the factors involved in the development of the disease, and to devise improved methods of treatment.

A second illness of unknown cause is Kawasaki disease. This *new* disease was reported first in Japan and has been recognized in this country since 1974. Most of these children have fever, conjunctivitis, red lips, strawberry colored tongue, swelling and redness of the extremities with peeling of the skin, a rash that is primarily on

the torso of the body, and enlarged lymph nodes. They also may develop pneumonia, diarrhea, or meningitis. Peeling of the skin on the toes and fingertips usually occurs about 10 days after the onset of the illness. The disease may be caused by a bacterial toxin, but the cause has not been identified and research is needed in order to develop effective treatment and prevention.

Antiviral chemotherapy now has begun to become available. Several drugs have been proven to be of value in certain types of herpes infections. The drug, 5-IDU, has been used for herpes infections of the eyes, and adenine arabinoside is helpful in the treatment of herpes encephalitis and congenital herpes infections. Amantadine hydrochloride has been useful in selected populations for the prevention and treatment of respiratory illness caused by influenza A virus. Antiviral chemotherapy can be expected to expand during the 1980s. Already improved drugs for herpes are being tested in patients. Because of the importance of herpes encephalitis and congenital herpes infection of the newborn, the availability of effective drugs is of utmost importance and worthy of intensive research. Other drugs are under study for the treatment of chronic hepatitis and varicella-zoster virus infections which include not only chicken pox but also shingles. Severe viral illnesses of the nasopharynx, lungs and gastrointestinal tract also can be expected to be targets for further studies during the 1980s.

Hepatitis B testing probably will be expanded for certain groups of people in the United States, particularly those who have come from China and other parts of Asia where there are very high rates of virus carriers. Increased use of hepatitis B immune globulin should help reduce the spread of this infection to the newborns of mothers who carry the virus. The association of hepatitis B infection with primary cancer of the liver has been well established, but examination of the nature of this relationship has been hampered by inability to grow the virus. This problem requires intensive investigation in the 1980s because of its importance to the control of hepatitis and to our understanding of the role of viruses in inducing cancer.

Group B streptococcal disease is extremely important in newborns. Several studies indicate that as many as 3 to 5 of every 1000 babies have severe Group B streptococcal infection which they acquire from their mothers at the time of birth. About half of these infections are fatal in spite of intensive treatment with antibiotics. New approaches to treatment and prevention are needed. Vaccine studies are already underway.

Development of new antibiotics for special needs will be extended in the 1980s. Problems, such as the failure of antibiotic therapy for Group B streptococcal disease in the newborn, need study. The changing resistance of organisms to antibiotics that are currently available will require continued search for new and better antimicrobials. Special emphasis will be placed on developing highly penetrating antibiotics to get to deep infections, such as those caused by Pseudomonas organisms in the mucous plugs of children with cystic fibrosis. *Fine tuning* of mixtures of antibiotics for special disease conditions will be extended by intensive laboratory and clinical research activities, so that adequate therapy for important and often fatal illnesses will be available. New potent antifungal drugs will be needed to broaden the chemotherapeutic approaches available for these infections.

Rapid viral diagnostic methods are becoming extremely important and will require further expansion in order to take advantage of new antiviral drugs likely to be developed in the 1980s. To use the appropriate drug and institute the appropriate care, it is necessary to have rapid, accurate diagnostic kits. The traditional techniques of virus isolation and detection of antibody to diagnose viral illnesses are too slow and inefficient for optimum use of antiviral chemotherapy. Thus, heavy emphasis must be placed on the development of new rapid techniques for the detection and identification of viruses in tissues and specimens without the use of cultures or classic antibody measurements. New methods such as ELISA IgM techniques, *flow-through* radioantigen assay, direct fluorescence and electron microscopy could be perfected and made available to make rapid viral diagnosis possible.

Increased information will be needed on both toxoplasmosis and cytomegaloviruses. Infections caused by these agents are known to produce severe damage to the developing fetus when women acquire the infections during pregnancy. Cytomegalovirus alone accounts for more than 3000 brain damaged newborns in the United States each year. The frequency of these problems requires investigations in a variety of populations. Then, attempts to interrupt the spread of the illnesses, the possible use of vaccines, or intensive serum testing can be evaluated properly and instituted on the basis of need. The cost/benefit/risk comparisons will have to be known for these illnesses, so that appropriate utilization of resources can be assigned. In addition, better methods for treatment will be needed for both maternal and congenital infections.

Slow virus diseases warrant special attention in the 1980s. Illnesses, such as progressive rubella panencephalitis and progressive multifocal leukoencephalopathy, are caused by common virus infections, but in certain individuals the infections spread with severe damage to the brain. We will need a better understanding of how these infections normally are controlled and why in certain individuals the virus spreads and causes severe illness and death. Research on neurological diseases of unknown cause will emphasize attempts to detect slow viruses as potential etiologic agents. Similar studies will be needed on other diseases of unknown etiology, including diabetes, ulcerative colitis, Crohn's disease and many other illnesses. New techniques using virus probes and monoclonal antibody will be needed for these studies.

The prevention of herpes in the newborn and recurrent genital herpes in adults will be a prime target in the decade to come. Genital herpes virus infections are occurring at a rate of at least 300,000 new cases per year in the United States. At present about 1 in 100 to 300 pregnant women has herpes infection during pregnancy, and transmission of the disease to the child at the time of birth may result in a severe fatal illness in the newborn. The infection is recurrent in adults and is often painful and incapacitating. There is a great need for methods for early diagnosis, treatment and prevention of genital herpes.

The control of otitis media, a common childhood infection also seen in adults, warrants intensive investigation in experimental animals and in children. Recent studies suggest that more information on the drainage of the middle ear may be important in understanding the development of this disease. This should result in improved control or prevention of these infections.

Meningitis caused by Haemophilus influenzae type b is the most frequent type of brain infection in children. Each year there are approximately 30,000 cases in the United States. Unfortunately, in approximately 20% of the cases, the bacteria are now resistant to penicillin. Further information is needed on this important disease, so that new antibiotics and possible vaccines may be developed in the 1980s. The vaccines will have to be potent in very young children as well as older children.

New tests for the rapid diagnosis of sepsis (bacterial infection in the blood) are being studied. These important methods will be needed for the rapid diagnosis of this life-threatening problem in newborns as well as in older children and adults.

Improvement is needed in the quality and reproducibility of laboratory tests for viral and other antibodies. While these tests are very reliable in research laboratories, some are still quite unsatisfactory when conducted by routine laboratories. Simplification of the tests, improved training of personnel, the use of reference reagents and frequent monitoring of diagnostic laboratories will be necessary to improve these test results.

The toxic shock syndrome was recognized recently and occurs primarily in older girls and women. It was particularly frequent among women who used new super absorbent tampons. The disease is thought to be associated with the growth of certain strains of toxin producing staphylococci in the vagina. These tampons have been removed from the market and intermittent use of tampons is being recommended. Further studies will be needed on the cause of this disease and optimal methods for prevention.

Most posttransfusion hepatitis in the United States is caused now by Non-A, Non-B viruses. This is because blood now routinely is tested for hepatitis B and antigen positive units are rejected. In addition, there is increased selection of voluntary donors. With the decrease in hepatitis B following transfusions, it has become apparent that Non-A, Non-B hepatitis viruses are important causes of hepatitis. Several candidate viruses have been identified. It will be necessary to develop sensitive tests for these viruses so that blood can be screened more completely prior to use for transfusions.

Immunizations may be particularly valuable when they are available for prophylaxis. Better influenza A and B vaccines are needed since current vaccines are not completely effective. With the control of influenza A and B, one could also expect fewer cases of Reye's syndrome, since there is a clear association between influenza and this disease.

Meningitis, caused by Group B meningococci, is the most frequent type of this disease seen in the United States. While vaccines have been produced for Groups A and C, research will be needed to develop potent vaccines for Group B infection in the 1980s.

The development of effective respiratory syncytial vaccines for administration to infants will be important in order to prevent the severe respiratory illness that occurs most commonly in very young infants. Vaccines tested to date have not been effective in young infants. New approaches will be needed for developing these vaccines in the 1980s.

Enteric viral vaccines for rotaviruses will be very important for prevention of diarrhea in infants and young children not only in the United States but in many other parts of the world where infant diarrhea carries a high mortality rate. Various strains of these viruses will have to be identified and characterized, and certainly, the task will not be easy. Nevertheless, the development of vaccines for these serious illnesses will be of great public health value.

Varicella-zoster (chickenpox) vaccines are under study in the United States and Japan. At this time, the vaccines are being investigated mainly in immunosuppressed children and children with leukemia or other malignancies. They are being used to immunize such children, so that if they are exposed to natural varicella at a later time they will not develop the often severe, usually fatal illness that is known to occur in immunosuppressed patients. If the vaccine proves to be effective and safe, it is possible that it also may be used in the general population at some future date. If used in children the vaccine may not only prevent chickenpox, but it also may reduce the frequency of Reye's syndrome that is frequently associated with varicella virus infection. It also may prevent or modify shingles.

Vaccines for cytomegalovirus (CMB) using live attenuated virus are already under evaluation by several groups of researchers in the United States and abroad. Preliminary studies have been conducted in normal volunteers. High risk groups also have been immunized, including patients with renal transplants who not infrequently become infected with CMV, which appears to increase the rate of rejection of the kidney transplants. The vaccine eventually may be available for immunization of women of childbearing age to prevent congenital infection with CMV. The importance of CMV in blood used for transfusions also has been demonstrated by recent studies. If donor blood is tested for antibody to CMV and only antibody negative blood is used, the chance of transmission of CMV by the transfusion to newborn children or to immunosuppressed patients is reduced significantly. It is possible that immunization of donors who do not have antibody may prevent natural CMV infection and stimulate antibody. This would make their blood particularly valuable for newborns and immunosuppressed patients.

Vaccines for hepatitis B (serum hepatitis) have been tested and could be of value to children in the third world where horizontal transmission in the first years of life is a major means of infection with this virus. It appears that vaccines for hepatitis A are likely to be available in the near future since the virus has now been grown in tissue culture. While hepatitis A is not a major problem in children in the United States, it is important in certain populations where transmission is frequent and hepatitis is a significant medical problem.

Gonorrhea is one of the most frequent venereal diseases in the world, and its occurrence is increasing in children as well as in adults. Preliminary studies suggest that it may be possible to prepare an effective vaccine for gonorrhea. This vaccine is prepared from a subfraction of the bacteria that causes the disease. If this or similar vaccines are effective, they will be of great value for this significant public health problem.

The major international problem of malaria may be affected significantly by the development of vaccines against the various strains of the malaria parasite. These immunization programs would be of particular importance in areas of the developing countries of the world where malaria continues to be widely prevalent.

Vaccines for pertussis (whooping cough) have been available for about 50 years. Purified vaccines with less side effects are needed. Research on subcellular, soluble vaccines are already underway and should result in a valuable improvement in this product.

Excellent vaccines are used now for polio and measles. Advances in the temperature stability of these vaccines should make it easier to transport and store these vaccines.

Immunization is a key to the goal of prevention of human diseases that have been known and feared throughout the centuries. With continued support for research and delivery of health services, we can look forward to many important advances in this decade.

Summary

Many important advances in research were made in the 1970s in the field of infectious diseases and immunization. Most of these already have been applied to clinical practice in the United States. Some of the advances in infectious diseases include diagnostic methods for detection of hepatitis A and B. These tests make it possible to exclude hepatitis B containing blood and thus prevent serum hepatitis associated with the use of this blood in transfusions. They also facilitate the use of hyperimmune gamma globulin for the protection of newborns exposed to hepatitis B from their mothers. Other advances have resulted in the reduction and almost complete elimination of subacute sclerosing panencephalitis through immunization programs for measles. New antibiotics have been developed for life-threatening diseases, such as bacterial endocarditis, pneumonia, abdominal infections, bone and joint infections, and neonatal meningitis. Diagnostic tests for diarrhea in infants and young children caused by rotaviruses have been introduced. Chlamydial infections were found to cause pneumonia in infants as well as urithritis and pelvic infections in older children and adults, and studies were initiated on approaches to diagnose, treat and prevent these diseases. Epstein-Barr virus was recognized as the cause of not only infectious mononucleosis but also childhood malignancy, Burkitt's lymphoma and other lymphomas. Legionnaire's disease was shown to be caused by a microorganism and antibiotics were used for treatment.

In the 1970s, immunizations provided great advances in clinical medicine including the eradication of smallpox throughout the entire world and the development of a highly successful rubella immunization program in the United States as well as outstanding measles and polio immunization efforts. These programs resulted in greatly reducing the number of cases of these diseases in the United States.

Meningococcal vaccines were developed for Groups A and C. Mumps vaccine was combined with measles and rubella to provide *triple* protection for children. The release of a pneumococcal vaccine was of particular importance to children over 2 years of age who had sickle cell anemia or nephrotic syndrome. A new human diploid rabies vaccine was developed requiring only five injections. This is only a

partial list of the advances of the 1970s in infectious diseases and immunizations that are available now to the children of the 1980s.

Prospects for the 1980s are extremely good. Continued intensive research activities in a number of areas should provide important opportunities for progress. For Reye's syndrome, it will be important to identify co-factors involved in the development of this disease. Kawasaki disease also requires research to uncover the cause of the disease so that effective treatment and prevention may be initiated. Research in antiviral chemotherapy should provide a number of new drugs for treatment of important viral infections, such as herpes encephalitis, congenital herpes, chronic hepatitis, and possibly, shingles. Hepatitis B testing may be expected to expand along with tests for hepatitis A and Non-A, Non-B hepatitis. Group B streptococcal disease of newborns will be studied to provide new approaches to treatment and prevention of this disease. New antibiotics will be developed for special needs including highly penetrating antibiotics for infections, such as those caused by Pseudomonas in children with cystic fibrosis. New potent antifungal drugs will be required to provide additional therapeutic approaches for these infections. Rapid viral diagnostic methods will have to be greatly improved so that appropriate antiviral drugs can be selected for patients experiencing certain viral diseases. Increased information will be needed on toxoplasmosis and cytomegalovirus infections during pregnancy to determine the frequency with which these infections cause congenital disease and damage, and to determine what methods can be devised for their prevention. Slow virus diseases will be worthy of special study, so that we can learn how these infections normally are controlled, and why, in certain patients, the virus spreads to cause severe illness and death. The prevention of herpes in the newborn and recurring herpes will be valuable because of the increasing rates of genital herpes in pregnant women. The control of otitis media will be extremely valuable and worthy, since this is a very common infection in children. It will be particularly important to study meningitis caused by Haemophilus influenzae type b in order to develop new antibiotics and possibly vaccines. Rapid tests for sepsis will be needed so that appropriate treatment with antibiotics will be started early in the course of disease. Improved serological tests for viral antibodies will permit reliable identification of susceptible individuals, immunization of those at risk, and documentation of infections. Methods for prevention of the toxic shock syndrome will be developed and the viruses that cause Non-A, Non-B hepatitis will be studied and probably identified.

Immunizations should receive particular emphasis and support in the 1980s, since they can prevent the occurrence of a number of important diseases. Some of the vaccines that need to be developed include: better influenza A and B vaccines, Group B meningococcal vaccines to control the most frequent type of meningitis in the United States, effective vaccines for respiratory syncytial virus to protect young infants from these severe respiratory infections and enteric viral vaccines for rotaviruses to reduce the frequency of diarrheal disease in infants and young children. Varicella-zoster vaccines are being evaluated now, and their study should be pursued so that potent methods will be available for preventing severe varicella in immunosuppressed children or children with various types of malignancies. These vaccines also could be of importance in the general population. Vaccines for the control of

cytomegalovirus will require study in greater detail to determine if these are effective in the prevention of congenital infection with this virus and in reducing the problem with cytomegalovirus in renal transplants. Vaccines for hepatitis B will be of particular importance in certain parts of the world where horizontal transmission is the means of spreading this infection. Hepatitis A vaccine will be useful in certain populations where transmission is frequent and the disease is a significant medical problem. The development of an effective vaccine for the prevention of gonorrhea is also of prime importance. The major problem of malaria in many parts of the world should be an important target, since development of vaccines against various strains of the malaria parasite would be of great international value. A purified vaccine for pertussis (whooping cough) should be developed to eliminate serious side effects. Lastly, more stable vaccines for polio and measles will be of great value to prevent loss of potency on transport or storage.

The opportunities for the prevention and control of infectious diseases in the 1980s are realistic and ready to be pursued. It will be necessary to have continued adequate funding for both basic and clinical research to support the implementation of the research findings and to take advantage of the medical advances that should come to us in the 1980s.

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